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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,891	11/27/2001	Bruno Paquin	5593-00300	1267

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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	10

DATE MAILED: 04/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,891	PAQUIN ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *06 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/31/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's preliminary amendment filed on July 6, 2001 in Paper No. 9 is acknowledged and has been entered. Claims 1-6 and 8-14 have been amended. Claims 1-14 are pending.

Sequence Listing

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR n1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth: The specification contains sequences at page 10 not represented by a sequence identifier (SEQ ID NO:). Appropriate correction is necessary.

Specification

3. The disclosure is objected to because of the following informalities:

(a) The disclosure is objected to for "In the claims". The claims page should begin with a sentence of which the claims will be an object such as "I (or We) claim:", "The invention claimed is:" (or the equivalent) not simply "Claims" or "In the claims" (see MPEP608.01(m)).

Appropriate correction is required.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 9-14 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 9-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claim 9-14 provides for the use of a library of oligonucleotides, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims1, 4, 6, 8-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gorenstein et al. (US 6,423,493, effective filing date: October 26, 1998) in view of Rampersad et al (US 5830,712, publication date: November 3, 1998). Regarding claims 1 and 8, Gorenstein et al teach an oligonucleotide library and process for generating a library of oligonucleotides that are specific for a given nucleic acid, comprising: (a) generating random oligonucleotides, wherein said oligonucleotides are of a uniform length comprising a single stranded, central segment of randomly varied bases and flanking segments of defined sequences on each side of the central segment (col. 2, lines 62-65 and SEQ ID NO: 1; col. 13 and 14); (b) hybridizing the random oligonucleotides with a nucleic acid-containing template of biological origin under conditions that enable the formation of duplexes; (c) eliminating non-specific duplexes; (d) separating the hybridized oligonucleotides from the duplexes obtained in step (c) and amplifying the hybridized oligonucleotides ((col. 3, lines 3-12) and Example 1, beginning at col. 8, line 28 to col. 10, line 19). The reference of Gorenstein et al. differs from the instant invention in that Gorenstein et al. do not expressly teach wherein a blocker is added to the duplexes to avoid hybridization of undesirable nucleic acid sequences. However, the specification does teach wherein a filter binding method is utilized numerous times as a selection process to separate hybridized duplexes from non-specific sequences.

In a general teaching, Rampersad et al teach a method of preparing specific cDNA libraries, i.e., cDNA libraries rich with respect to certain cDNAs, the method comprising selectively inactivating undesirable nucleic acid members to enable isolating of the desired cDNA by adding a blocker to the sample which selectively associates with the undesirable

nucleic acids in the sample thereby preventing such nucleic acid from participating in any further processing of the sample ((col. 2, lines 18-25). Rampersad et al teach that the method is advantageously because it allows for the selective inactivation of nucleic acids that are intimately related to the desired nucleic acids in a given sample, the determination of which can be masked by the presence of the undesired nucleic acids (col. 2, lines 25-30, col. 4, line 59 to col. 5, line 2). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention to have been motivated to have modified the process of preparing an oligonucleotide library as taught by Gorenstein et al to encompass a blocker to the nucleic acid duplex instead successive rounds of selection. One of ordinary skill in the art would have been motivated to do so for the benefits of selectively inactivating undesirable nucleic acids from the sample, thus increasing the isolation of desired nucleic acids as taught by Rampersad et al.

Regarding claim 4, Gorenstein et al teach the process of claim 1, wherein the central segment comprises 22 bases and wherein the flanking segments comprise 22-23 bases (see SEQ ID NO: 1, col. 13 and 14 and col. 8, lines 36-38).

Regarding claim 6, Gorenstein et al teach the process of claim 1, wherein the nucleic acid-containing template comprises at least one of genomic or synthetic DNA or RNA (col. 4, lines 41-45).

[1]Regarding claim 9, 10 and 11, Gorenstein et al teach wherein the library of oligonucleotides may be used to inhibit gene function or as a diagnostic tool (col. 5, lines 14-24). The use of the oligonucleotide library as a diagnostic kit is an inherent property of the oligonucleotide library of Gorenstein et al.

[1]Regarding claim 12 and 13, Gorenstein et al teach wherein the library of oligonucleotides are bound to a solid support wherein the solid support is a chromatographic media (column or nitrocellulose filter) or microspheres (beads) (col. 7, lines 21-31 and col. 9, lines 19-26).

10. Claims 2, 3 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gorenstein et al in view of Rampersad et al as previously applied above, and further in view of Liang (US 5,827,658, October 27, 1998). Regarding claims 2, 3 and 7, Gorenstein et al in view of Rampersad et al teach an oligonucleotide library and process for generating a library of oligonucleotides comprising: generating random oligonucleotides, wherein said oligonucleotides are of a uniform length comprising a single stranded, central segment of randomly varied bases and flanking segments of defined sequences on each side of said central segment; hybridizing the random oligonucleotides with a nucleic acid-containing template of biological origin under hybridization conditions that enable the formation of duplexes and using blockers to avoid hybridization of undesirable sequences; eliminating non-specific duplexes; separating the hybridized oligonucleotides from the duplexes obtained in the prior step and amplifying the hybridized oligonucleotides.

The process of Gorenstein et al and Rampersad et al differs from the instant invention in that the references do not teach wherein the process further comprises subtracting between two different oligonucleotide libraries which contain similar sequence motifs. In a method for the isolation of amplified genes, Liang teaches the uses of subtractive hybridization of two different

[1] Since the claims do not recite any method steps, the preceding rejections are based on the Examiner's interpretation

libraries which contain similar sequence motifs. Liang teaches wherein the method comprises generating single stranded versions of oligonucleotide libraries (OL1=oligonucleotide of interest) and (OL2=oligonucleotides from normal tissue) annealing the OL1 with an excess of OL2 under hybridization conditions; partitioning double-stranded hybrids (OL1:OL2) and single stranded OL2 from single stranded OL1, wherein said partitioning is carried out using streptavidin or avidin and biotin; amplifying the single stranded OL1 and repeating the steps to obtain OL1 oligonucleotides with reduced affinity for OL2 (col. 3, lines 19-49). Liang teaches that the process provides a simple and more sensitive method of identifying single stranded oligonucleotides libraries representing amplified genes (col. 1, lines 63-65), especially amplified genes in tumor specimens (see background of invention, col. 1) and ways of estimating their copy number (col. 1, lines 63-65) which can be correlated to the severity of a pathogenic state, to its prognosis or to treatment efficacy (abstract). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention to have been motivated to have modified the process of generating oligonucleotides libraries as taught by Gorenstein et al in view of Rampersad et al to encompass steps of subtracting between different oligonucleotides libraries having similar sequence motifs. One of ordinary skill in the art would have been motivated to do so for the advantages taught by Liang of identifying oligonucleotides libraries representing amplified genes and ways of estimating their copy number which can be correlated to the severity of a pathogenic state, to its prognosis or to treatment efficacy.

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of the claims.

11. [1]Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gorenstein et al in view of Rampersad et al as previously applied further in view of Schmidt et al (WO 98/15651, April 16, 1998). Gorenstein et al in view of Rampersad et al teach an oligonucleotide library and process for generating a library of oligonucleotides comprising: generating random oligonucleotides, wherein said oligonucleotides are of a uniform length comprising a single stranded, central segment of randomly varied bases and flanking segments of defined sequences on each side of said central segment; hybridizing the random oligonucleotides with a nucleic acid-containing template of biological origin under hybridization conditions that enable the formation of duplexes and using blockers to avoid hybridization of undesirable sequences; eliminating non-specific duplexes; separating the hybridized oligonucleotides from the duplexes obtained in the prior step and amplifying the hybridized oligonucleotides. The process of Gorenstein et al. in view of Rampersad et al differs from the instant invention in that the references do not teach wherein the oligonucleotides are hybridized to nucleic acid arrays. Schmidt et al teach random oligonucleotide libraries wherein said oligonucleotides of the library are hybridized to an array (page 10, line 6-11). Schmidt et al teach that since the oligonucleotide libraries are all immobilized on an array, there will be no cross hybridization (page 10, lines 6-11). Therefore, in view of the foregoing, one of ordinary skill in the art at the time of the claimed invention would have been motivated to have modified the process of generating an oligonucleotide library as taught by Gorenstein et al. in view of Rampersad et al to encompass hybridization to an array. One of ordinary skill in the art would have been motivated to do so for the benefit of alleviating or preventing any cross hybridization as taught by Schmidt et al.

Conclusion

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Wilder

CYNTHIA WILDER
PATENT EXAMINER

4/2/04